Patient/sex	Approximately Weight (kg)	Initial busulfan dose (mg/kg)	Clearance at busulfan (ml/kg/min)	AUC(0-inf) after the first dose (μMol.min)	Dose adjustment	Adjusted dose	AUC(0-inf) 6h month dose (μMol.min)	Total received dose (mg/kg)
1/F	4/5.1	0.8	3.95	823 (1021)	No change	NA	ND	12.8
2/M	9/6	1	4.87	833	No change	NA	ND	16
3/F	14/2	0.8	2.98	1103(1378)	Decrease	0.66	ND	11.35
4/M	10/5.9	1	3.09	1315	Decrease	0.66	ND	12.8
5/M	8/6.9	1	3.1	1207	No change	NA	ND	16
6/M	8/7.3	1	4.77	1077	No change	NA	ND	16
7/F	0.7/7.5	1	NA	1986	Decrease	0.5	ND	11.93
8/M	9/10	1	7.1	1170	Decrease	0.9	ND	15.1
9/F	1.5/11.5	1	3.3	1264	Decrease	0.66	768	12.8
10/F	9/5.4	1	2.8	1161	Decrease	0.71	948	13.3
11/M	2.9/13.8	1	3.1	1264	Decrease	0.79	980	13.6
12/F	12/10	1	4.72	1099	No change	NA	ND	16
13/F	7/7.2	1	4.37	889	Increase	1.25	ND	19.25
14/M	4/6.2	0.8	4.12	916(992)	Increase	0.92	ND	13.9
Median	1.9/5.9		3.4	1234				13.75
Mean ±SD			3.62±0.94	1234±293				14.1±1.98

AUC: area under concentration-time curve, ND: not done, NA: not available, SD: standard deviation, *calculated values from normalized AUC for 1 mg/kg busulfan, Pt: patient, M: male, F: female

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RETROSPECTIVE COMPARISON OF ALLOGENEIC STEM CELL TRANSPLANTATION (SCT) IN PEDIATRIC PATIENTS UTILIZING PERIPHERAL BLOOD STEM CELLS (PBSC) VS BONE MARROW (BM)

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G-CSF mobilized PBSC are increasingly used as a source of hematopoietic stem cells (HSC) for allogeneic SCT. Randomized studies in adults suggest benefits using PBSC related to early engraftment, reduced acute toxicity and lack of increase in acute graft-vs-host disease (GVHD) despite the increase in T-cell dose administered with PBSC. Reports comparing chronic GVHD following SCT using PBSC vs BM have varied. Pediatric (vs adult) recipients of allogeneic SCT have lower rates of acute and chronic GVHD, as well as reduced risk for acute toxicity. We report a retrospective comparison of 76 pediatric patients with hematologic malignancies, 15 received allogeneic PBSC from matched related (n= 11) or unrelated donors (URD, n= 4) from 3/2000 through 9/2002. 61 received BM from matched related (n= 51) or URD (n= 10) from 6/1992 through 7/2002. PBSC donors received G-CSF (10 mcg/kg/d x 4d) for HSC mobilization. Cytoreduction therapy for all patients was fractionated total body irradiation (150 cGy x8 = 1200 cGy) + etoposide (1000 mg/m2 x1) + cyclophosphamide (60 mg/kg x3). Growth factor support with G-CSF was routinely administered beginning on day +7. GVHD prophylaxis was similarly uniform (Cyclosporine A and reduced methotrexate-days 1, 3 & 6). All URD recipients also received ATG (20 mg/kg x4 post SCT) and 11 URD recipients received tacrolimus substituted for Cyclosporine A. Patients treated with other cytoreduction protocols or alternative GVHD prophylaxis regimens were excluded. Although retrospective, non-randomized and longer follow-up exists for the BM recipients, this analysis of PBSC vs BM in Pediatric allogeneic SCT recipients suggests results similar to larger randomized studies in adults-reduced 100 day mortality without increased acute GVHD. Despite shorter follow-up, chronic GVHD was significantly greater in PBSC recipients. Longer follow-up is required to better assess true rates of recurrence and chronic GVHD after SCT with PBSC. A randomized trial will require multi-center participation. Allogeneic SCT using PBSC in pediatric patients appears to be an acceptable alternative to BM.

	PBSC (n= 15)	BM (n = 61)
*Age (yrs)	13 (14, 1-20)	10.2, (9.7, 0.5-23)
M/F	5/10	44/17
Diagnosis ALL	8 (53 %)	41 (67 %)
AML	4 (27 %)	16 (26 %)
Other	3 (20 %)	4 (7 %)
**Days to ANC >500/ul	13.5, (14, 10-16)	20.1, (17, 11-144)
**Days to Plt >20,000/ul	27, (28, 7-37)	35.3, (24, 11-222)
**Length of Stay for SCT	25.3, (26, 19-34)	33.2, (26, 9-123)
100 day mortality	1	20
Acute GVHD Gr II-IV	5	12
#Chronic GVHD	6	6
Recurrences	0	9
*Mean, (Median, range)		
**Mean, (Median, range) in evaluable patients		
# (P <0.05)		

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OUTCOME OF PEDIATRIC PATIENTS WHO UNDERGO HEMATOPOITIC STEM CELL TRANSPLANTATION (HSCT) FOR MONOSOMY 7 AND OTHER CYTIOGENETICALLY ABNORMAL MYELODYSPLASTIC SYNDROMES (MDS) OR ACUTE NON-LYMPHOBLASTIC LEUKEMIA (ANLL) A SINGLE INSTITUTION EXPERIENCE

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From March 1992 to September 2002 sixteen patients were diagnosed with cytogenetically abnormal MDS/ANLL. Our objective is to report the outcome of these patients after they received an HSCT. Of the 16 patients, there 9 males and 7 females. Mean age at diagnosis is 7.3 years, median 6.6 (1.0-16.6), Race Caucasian (n=9), African American (n=2), Hispanic (n=4) and 1 other. Type of HSCT Unrelated umbilical cord (n=8), matched sibling (n=3), matched unrelated (n=4) and autologous with 4-HC purged marrow (n=1). Eleven patients had the diagnosis of MDS and 5 ANLL; 8 were primary and 8 were secondary. The cytogenetic abnormalities include: Monosomy 7 (n=10), Monosomy 5 (n=1), Monosomy 5, 7 (n=1) Trisomy 8 (n=1), t (6-9) (n=2) and t (8-16) (n=1). Ablation was TBI 150cGy BID x 8 doses, VP-16 (VP) 1000mg/m2/day x1 day and Cycophosphamide (Cy) 60 mg/kg/day x 3 days (n=9); Busulfan (BU) 1mg/kg/dose x 16 doses, VP, Cy (n=5); and Fludarabine 25mg/m2/day x 6 days, BU 1mg/kg/dose x 8 and ATG 40mg/kg/day x 5 days n=(2). Cell doses infused MNC x 108/kg mean 0.3 (median 0.5, range 0.1-7.1) CD34+ cells x 106/kg mean 0.6, (median 1.8, range 0.3-16.2) GVHD prophylaxis included: CSA/MTX/ATG (n=10), CSA/MTX (n=3), CSA (n=2), none (n=1). The time to ANC>500 was mean 31days (median 22.5days), to platelets of >20.0 mean 36.5 days (median 37days) and platelets >50.0 mean 55 days (median 53 days). Grade I/II GVHD develop in (n=7) Grade III/IV (n=2), no GVHD (n=7). No chronic GVHD (n=13), Limited (n=1) Extensive (n=1) unknown (n=1). Other complications included: Interstitial pneumonia (n=1) Toxic Epidermolysis (n=1) Fungal Infection (n=2) Hemorragic Cystitis (n=2). The Event free survival at 4 years post transplant is 55% (95% CI 0.4-.07). HSCT for patients with MDS/ANLL with cytogenetic abnormalities can be an effective treatment, even when alternative donor sources are used.

SOLID TUMORS

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NS1 AND NS2 SUBPOPULATIONS OF BONE MARROW NATURAL SUPPRESSOR CELLS

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Natural suppressor (NS) cells are heterogenic population of early bone marrow haemopoietic precursors that play an important role in chronic GVHD and also in suppression of NK activity during tumor development. Proceeding on numerous literature data we have suggested that there are at least two NS subpopulations: NS1 and NS2 which are stimulated with IL-2 and IFNg or IL-3 and GM-CSF respectively. In this work we have tried to prove the existence of these two NS subpopulations. The bone marrow cells (BMC) of CBA mice were cultivated in concentration of 2x106/ml under standard cell culture conditions for 48 h. NS activity was judged on the ability of BMC culture supernatants to inhibit myeloma cell proliferation by MTT-test. We determined NS activity induced with IL-2 (NS1), IL-3 (NS2) or spontaneous (sNS). NK activity of mononuclear spleen cells was estimated by cytotoxic assay. TGFb was determined by ELISA. We have shown that sNS activity was not observed while NS1 and NS2 activity was determined and apparently it was connected with TGFb; production because of antiproliferative activity of supernatants corelated with TGFb concentration. Furthermore these supernatants inhibited NK activity for certain. Earlier we have shown that the most sNS activity is revealed in BMC